

IN THE CLAIMS

Please cancel non-elected claims 1-11, 13, 15, and 19, without prejudice. Please add the new claim 25. The following listing of claims replaces all prior listings.

1-11 (Canceled).

12. (Previously presented) A method for screening for molecules having an affinity for an active protein in a complex mixture of proteins from a biological source, employing a combinatorial chemical library comprising a plurality of members of the formula

$R^* (F - L) - X$

wherein:

X is a ligand having the same chemical structure for each of said members of said combinatorial chemical library,

L is a bond or alkylene or an alkyleneoxy chain linking group of from 1 to 6 alkyleneoxy groups, wherein said alkyleneoxy groups are of from 2 to 3 carbon atoms, which is the same in each of the members of said combinatorial chemical library;

F is a sulfonyl functional group reactive at an active site of a protein member, which functional group comprises the same reactive functionality in each of the members of said combinatorial chemical library, and

R is a group of less than 1kDal, that is different in each of the members of the combinatorial chemical library;

the * intends that R is a part of F or L; and

wherein members of said combinatorial chemical library have different on rates with said protein member; said method comprising:

(1) combining with said complex mixture of proteins, in an active form and an inactivated form, said combinatorial chemical library under conditions for reaction of said sulfonyl functional group with active proteins to form a conjugate;

(2) isolating conjugates from said active and inactivated complex mixture of proteins; and

(3) comparing conjugates formed with said active and inactivated complex mixtures of proteins;

whereby conjugates in said active complex mixture absent in said inactivated complex mixture are comprised only of active proteins reactive with members of said chemical combinatorial library.

13. (Canceled)

14. (Previously presented) A method for screening for molecules having an affinity for an active target protein in a complex mixture of proteins from a biological source, employing a combinatorial chemical library of activity based probes comprising a plurality of members of the formula

$R^* (F - L) - X$

wherein:

X is a ligand having the same chemical structure for each of said members of said combinatorial chemical library;

L is a bond or alkylene or an alkyleneoxy chain linking group of from 1 to 6 alkyleneoxy groups, wherein said alkyleneoxy groups are of from 2 to 3 carbon atoms, which is the same in each of the members of said combinatorial chemical library,

F is a sulfonyl group that is the same in each member of said combinatorial chemical library; and

R is a group of less than 1kDal, that is different in each of the members of the combinatorial chemical library;

the * denotes that R is a part of F or L;
said method comprising:

- (1) combining a first portion of said complex mixture of proteins with said combinatorial chemical library under conditions for reaction of said sulfonyl group with active proteins in said complex mixture of proteins to form conjugates;
- (2) combining a second portion of said complex mixture of proteins, that has been inactivated, with said combinatorial library under the same reaction conditions as in (1)
- (3) isolating conjugates from said first and second portions of said complex mixture of proteins; and
- (4) comparing conjugates formed from said first portion of said complex mixture of proteins with conjugates formed from said second portion of said complex mixture of proteins to determine the degree of activity of the total target protein as compared to active target protein.

15 (Canceled).

16. (Previously presented) A method according to claim 14, wherein said members of said combinatorial chemical library of activity based probes have differing on-rates with respect to said active proteins.

17. (Previously presented) A method according to claim 14, wherein X is biotin, deiminobiotin, dethiobiotin, a vicinal diol, digoxigenin, maltose, oligohistidine, glutathione, 2,4-dinitrobenzene, phenylarsenate, ssDNA, ds DNA, a peptide, metal chelate, saccharide, rhodamine, fluorescein, or a hapten.

18. (Previously presented) A method according to claim 14, wherein X is biotin.

19. (Canceled).

20. (Previously presented) A method according to claim 14, wherein R is alkyl, heterocyclic, aryl, substituted aryl, amino acid, peptidyl, oligonucleotide, or a carbohydrate group.

21. (Previously presented) A method according to claim 14, wherein F is sulfonate, sulfate, sulfinate, or sulfamate.
22. (Previously presented) A method according to claim 21, wherein F is sulfonate.
23. (Previously presented) A method according to claim 14, wherein said second portion of said complex mixture of proteins has been inactivated by heating.
24. (Previously presented) A method according to claim 14, wherein said combinatorial chemical library of activity based probes comprises at least two of sulfonate 1 - sulfonate 11 and sulfonate 15 - sulfonate 17.
25. (New) A method according to claim 20, wherein heterocyclic is selected from a group consisting of pyridyl, substituted pyridyl, imidazole, pyrrole, thiophene, furan, azole, oxazole, and aziridine.